Arteriovenous fistulas aggravate the hemodynamic effect of vein bypass stenoses: An in vitro study

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Purpose: **The purpose of this study was to assess the impact of arteriovenous fistulas combined with varying degrees of stenosis on distal bypass hemodynamics and Doppler spectral parameters.**
Methods: **In an in vitro flow model bypass stenoses causing 30%, 55%, and 70% diameter reduction were induced 10 cm upstream of a fistula with low outflow resistance. Flow and intraluminal pressure were measured proximal to the stenosis and downstream of the fistula. The waveform parameters peak systolic velocity, end-diastolic velocity, pulsatility index, and pulse rise time were determined from midstream Doppler spectra obtained 10 cm downstream of the fistula. All measurements were carried out with open and clamped fistula.**
Results: **At 30% diameter reducing stenosis opening of the fistula induced a 12% systolic pressure drop across the stenosis but had no adverse effect on the Doppler waveform parameters. At 55% stenosis the pressure drop increased from 16% to 31% after fistula opening. This increased pressure drop was associated with a further reduction in peak systolic velocity, a decrease in pulsatility index, and an enhanced pulse rise time prolongation. Fistula opening at 70% stenosis increased the systolic pressure drop from 31% to 48% and had significant impact on all waveform parameters.**
Conclusions: **Distal arteriovenous fistulas enhance pressure loss across stenoses and affect downstream velocity waveform configuration. The presence of a combined fistula and a stenosis mimics the distal hemodynamic conditions of a more severe stenosis. Assessment of the hemodynamic impact of fistulas must be undertaken in the evaluation of in situ vein bypass stenoses. (J Vasc Surg 1996;24:1043-9.)**

In situ vein bypass surgery has become an established method for lower extremity revascularization.[1,2] Side branches of the saphenous vein, which are not identified and ligated during surgery, may persist as arteriovenous fistulas after surgery and cause shunting of blood from the bypass to the venous system.[3-5]

Fistulas causing up to 90% shunting are being compensated for by an increased inflow and have no adverse effect on bypass hemodynamics in patients without graft stenoses or inflow restrictions.[6,7] However, the perfusion pressure in peripheral vascular disease is determined both by the flow rate and the degree of luminal narrowing.[8] We therefore hypothesize that fistulas located downstream of stenoses may induce or enhance transstenotic pressure loss and distal ischemia of the extremity despite supranormal flow into the graft. Accordingly, the aim of this study was to evaluate the hemodynamic impact of fistulas located downstream of stenoses in an experimental pulsatile model in which bypass and fistula flow could be controlled. Furthermore we assessed the value of distal Doppler waveform parameters for discrimina-

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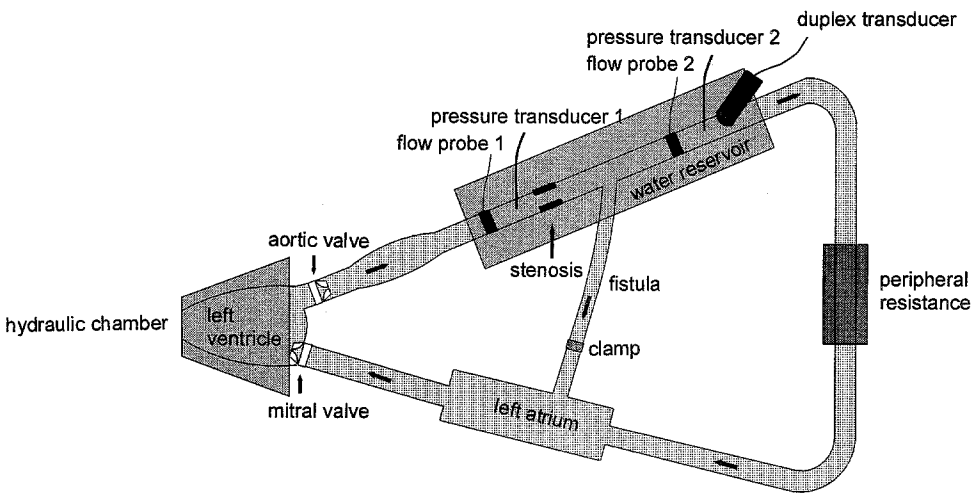

Fig. 1. In vitro flow model. Computer-controlled pulse duplicator is connected to 6 mm latex tube with adjustable central compliance and peripheral resistance. Varying degrees of stenosis can be induced 10 cm proximal to 4 mm side branch. Circulating fluid is blood analogous solution with dynamic viscosity of 4.2 cP.

tion between a hemodynamic impairment caused by a stenosis and by a fistula.

MATERIAL AND METHODS

In a computer-controlled flow model[9] a pulse duplicator (Vivitro Systems, London, Victoria, Canada) providing a pulsatile flow at a fixed heart rate of 72 beats/min was connected to a 6 mm inner diameter latex tube immersed in water. Symmetric stenoses 1 cm in length causing 30% (minor), 55% (moderate), and 70% (severe) diameter reduction corresponding to 51%, 80%, and 91% area reduction were induced by mounting plastic tubes of decreasing diameter inside the latex tube. A fistula was modeled by insertion of a 4-mm inner diameter side branch 10 cm downstream of the stenoses. The fistula outflow resistance was virtually zero. To simplify data interpretation collateral flow was not simulated. The circulating fluid was a methylcarboxycellulose solution with starch added to obtain acoustic properties comparable to those of blood. The dynamic viscosity was 4.2 cP (Fig. 1).

Volume flow (Q) was measured continuously by a Cardiomed CM-4000 Transit Time Flowmeter (Medistim, Oslo, Norway), and intraluminal pressure was continuously registered by a 5F SPC 350 MR Millar Microtip Catheter Pressure Transducer (Millar Instruments Inc., Houston, Tex.) proximal to the stenosis and distal to the side branch. The 8 mm flow probes were calibrated by cylinder and stopwatch technique. In each series flow and pressure signals of 12 cardiac cycles were A/D converted with a sampling frequency of 400 Hz and stored on a personal computer.

Velocity waveforms were simultaneously recorded in the center of the tube 10 cm distal to the fistula with a Vingmed Sound CFM-800 C duplex scanner (Vingmed Sound, Oslo, Norway) with a 6 MHz annular transducer at a Doppler angle of 60 degrees. The sample depth was 1 mm. Six subsequent recordings of four cardiac cycles were performed in each series and downloaded to a Macintosh computer. The following waveform parameters were calculated by means of a software package (Echo Disp 4.0, Vingmed Sound): peak systolic velocity (PSV), pulse rise time (PRT), and pulsatility index (PI = [peak systolic velocity − minimum diastolic velocity]/time average maximum velocity).

Before stenosis was induced, adjustment of the flow rate and peripheral resistance was made to produce a diphasic Doppler spectrum with a PSV of 90 cm/sec (Fig. 2).[6] This velocity waveform and model settings were used as reference for the subsequent geometric and hemodynamic changes.

The measurements were conducted with the fistula in clamped and open condition. The degree of shunting was controlled by regulating the outflow resistance of fistula and bypass. At 0%, 30%, and 55% degree of stenosis proximal flow was increased by 200% after the fistula was opened, and the variation in distal flow was kept below 10%. At 70% stenosis with closed fistula flow was reduced by 30%.[10] After fistula declamping proximal flow was increased by only 30%

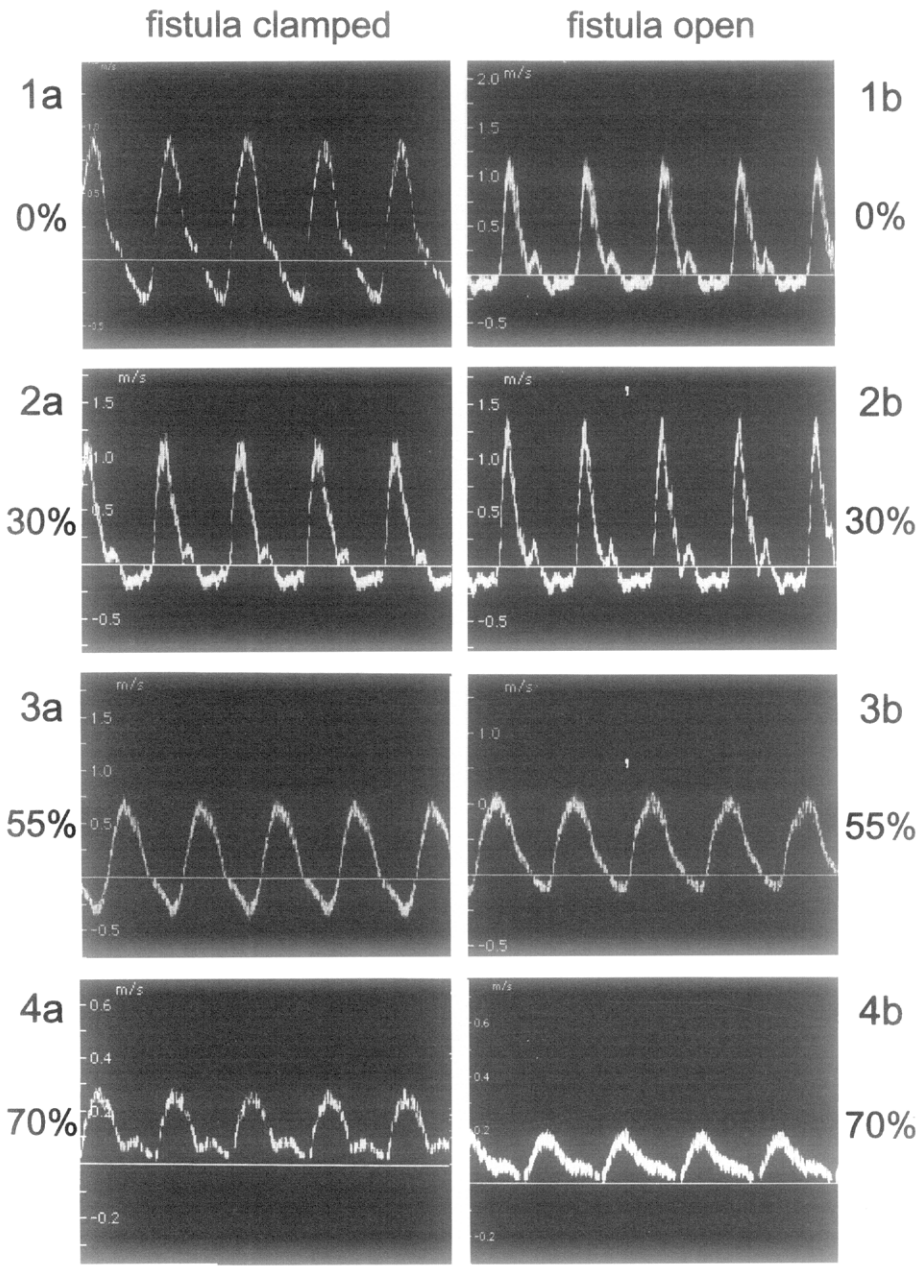

Fig. 2. Distal spectral Doppler waveforms. *1a,* 0% stenosis without fistula, *1b,* 0% stenosis with fistula, *2a,* 30% stenosis without fistula, *2b,* 30% stenosis with fistula, *3a,* 55% stenosis without fistula, *3b,* 55% stenosis with fistula, *4a,* 70% stenosis without fistula, *4b,* 70% stenosis with fistula. Severity of stenosis is stated as percentage diameter reduction.

and distal flow reduced by 30% to avoid nonphysiologic pressure increments upstream of the stenosis.

With increasing degree of stenosis the peripheral resistance was gradually reduced and the central compliance was increased by inserting additional large-caliber latex tubes between the pulse duplicator and the stenosis.

Statistics. Continuous variables in two groups were compared by the Mann Whitney rank sum test, and correlation between two continuous variables was estimated by Spearman's rank correlation analysis. A confidence limit of less than 0.01 was regarded as significant. Velocity waveform parameters are listed as median values and ranges.

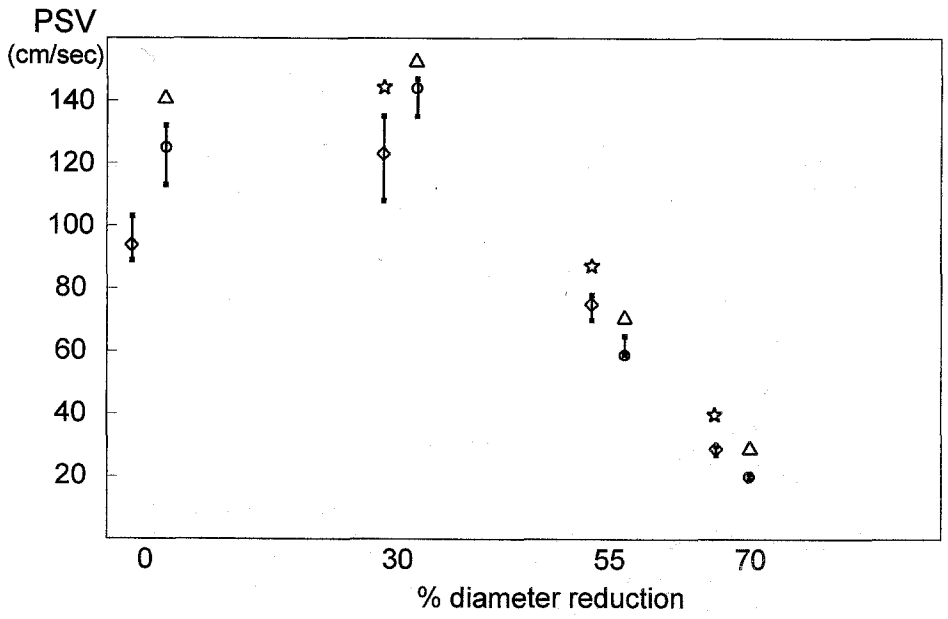

Fig. 3. Peak systolic velocity *(PSV)* related to degree of stenosis, ◇ without fistula, ○ with fistula. *$p < 0.01$ compared with 0% stenosis, △ $p < 0.01$ compared with series without fistula but similar degree of stenoses. Median values and ranges of six recordings.

Table I. Flow and pressure data

	Qproximal	*Qdistal*	*Pproximal*	*Pmean proximal*	*Pdistal*	*Pmean distal*	*Pressure drop (%)*
0% Closed fistula	186	177	101/43	62	100/40	61	1
0% Open fistula	536	182	120/35	63	117/32	63	2
30% Closed fistula	177	177	120/33	64	115/32	63	4
30% Open fistula	524	166	139/24	63	123/25	62	12
55% Closed fistula	230	216	111/59	79	93/50	67	16
55% Open fistula	586	199	120/38	69	83/28	48	31
70% Closed fistula	164	147	111/61	81	77/50	64	31
70% Open fistula	200	104	120/35	69	63/32	42	48

Qproximal, Proximal flow (ml/min); *Qdistal,* distal flow (ml/min); *Pproximal,* proximal systolic and diastolic pressure (mm Hg); *Pmean proximal,* proximal mean pressure (mm Hg); *Pdistal,* distal systolic and diastolic pressure (mm Hg); *Pmean distal,* distal mean pressure (mm Hg); *Pressure drop,* 1-ratio of distal systolic pressure and proximal systolic pressure. Median values of 12 cardiac cycles.

RESULTS

No stenosis. Opening of the fistula caused a 17 to 19 mm Hg increase in systolic pressure both proximal and distal to the stenosis induction site (Table I). Correspondingly PSV increased from 94 (89 to 103) cm/sec to 125 (113 to 132) cm/sec ($p = 0.004$) (Fig. 3), PI increased from 4.6 (4.0 to 5.5) to 6.1 (5.6 to 7.8) cm/sec ($p = 0.004$) (Fig. 4), and PRT was unaffected ($p = 0.8$) (Fig. 5) by fistula declamping.

Minor (30% diameter reducing) stenosis. Fistula declamping caused a proximal and distal systolic pressure increase and induced a 12% systolic pressure drop across the stenosis. PSV increased from 123 (108 to 135) cm/sec to 144 (135 to 147) cm/sec ($p = 0.005$), PI was not significantly affected ($p = 0.01$), and PRT remained unchanged ($p = 0.5$) (Figs. 3, 4, 5).

Moderate (55% diameter reducing) stenosis. During fistula clamping the systolic pressure drop was 16%, associated with reduced PSV (75 [70 to 78] cm/sec) and prolonged PRT (0.16 [0.16 to 0.18] sec) After fistula declamping the pressure drop increased to 31%, PSV decreased further to 59 (59 to 65) cm/sec ($p = 0.005$), PI was reduced to 3.0 (2.9 to 3.2) ($p = 0.006$), and PRT increased further to 0.20 (0.18 to 0.23) sec ($p = 0.005$) (Figs. 3, 4, 5).

Severe (70% diameter reducing) stenosis. During fistula clamping the distal pressure was mark-

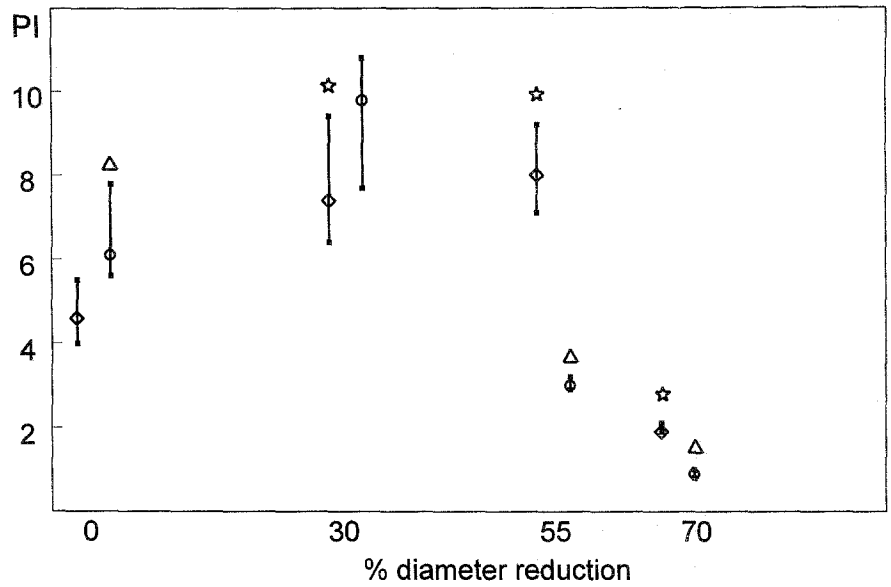

Fig. 4. Pulsatility index (PI) related to degree of stenosis, ◇ without fistula, ○ with fistula. *$p <$ 0.01 compared with 0% stenosis, △ $p < 0.01$ compared with series without fistula but similar degree of stenoses. Median values and ranges of six recordings.

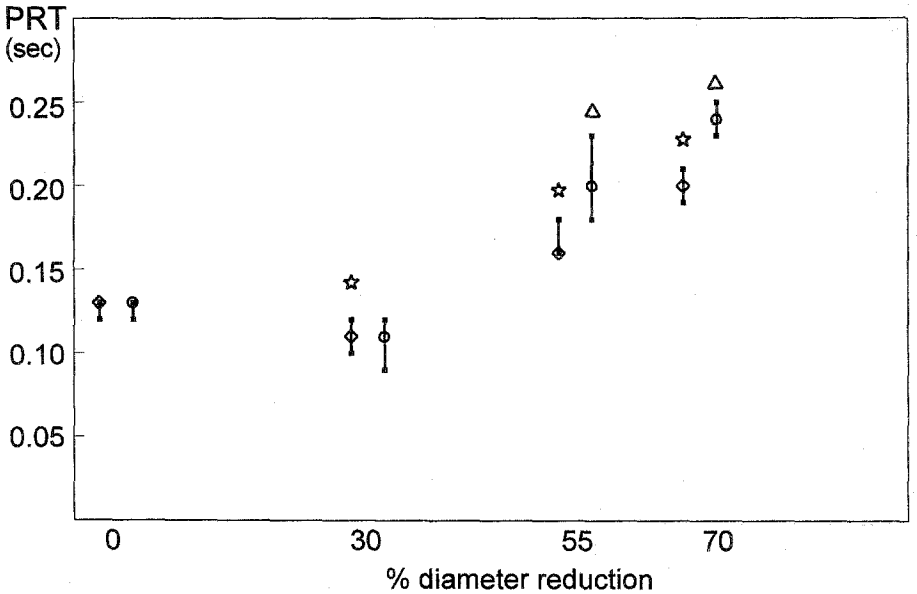

Fig. 5. Pulse rise time (PRT) related to degree of stenosis, ◇ without fistula, ○ with fistula. *$p < 0.01$ compared with 0% stenosis, △ $p < 0.01$ compared with series without fistula but similar degree of stenosis. Median values and ranges of six recordings.

edly reduced, diastolic flow reversal was absent, and all Doppler waveform parameters were affected. After declamping of the fistula the systolic pressure drop increased from 31% to 48%, PSV decreased from 29 (27 to 30) cm/sec to 20 (19 to 21) cm/sec ($p =$ 0.003), PI decreased from 1.9 (1.9 to 2.1) to 0.9 (0.8 to 1.0) ($p = 0.005$), and PRT increased from 0.20 (0.19 to 0.21) sec to 0.24 (0.23 to 0.25) sec ($p =$ 0.003) (Figs. 3, 4, 5).

Correlation between waveform parameters and pressure. PI showed a linear correlation with the distal systolic pressure ($R = 0.83, p < 0.001$), and PRT correlated with the pressure drop across the stenosis ($R = 0.80, p < 0.001$).

DISCUSSION

Residual arteriovenous fistulas increase proximal flow rate but rarely impair distal hemodynamics in in situ vein bypasses without stenoses.[5,6] Because pressure reduction across stenoses is flow-dependent,[8] fistulas may, however, have hemodynamic impact in strictured vein bypasses.[4]

In this in vitro study the pressure drop across a stenosis and the distal Doppler waveform configuration were affected by opening of a fistula located downstream of the stenosis. The impact of fistula opening corresponded to the impact of increasing the degree of stenosis. Thus a combined stenosis and a downstream fistula affected distal bypass hemodynamics in the same way as a more severe isolated stenosis. In the clinical situation lesions in the in- or outflow tract may increase the distal pressure reduction, whereas collateral flow may decrease the pressure drop.

The feasibility to adjust central compliance and peripheral resistance in response to induction of stenosis and fistula declamping was limited. Despite these drawbacks we obtained Doppler spectra of good resemblance to those seen in peripheral bypasses. The pressure and flow rates were within the physiological ranges except at 70% degree of stenosis, where only a minor flow increase could be accomplished and where distal flow reduction was unavoidable after fistula opening. If a further flow increase had been possible, fistula declamping would probably have caused an even more pronounced pressure drop.

The impact of fistulas located upstream of stenosis was not assessed in this study. Because flow through the stenosis is unaltered in these cases, the effect must be assumed to be minor, unless flow is extremely high.

Because residual arteriovenous fistulas are found in up to 75% of in situ vein bypasses[6,13] and graft-related stenoses develop in 20% to 30% within the first year[14-16] after surgery, the combination of fistulas and stenoses is not an uncommon finding. Although bypass failure occasionally has been attributed to large arteriovenous fistulas,[17] most authors are in favor of a conservative approach towards fistulas.[1,5,18] Fistula ligation is recommended only in case of hemodynamic impairment[4] or persistant local symptoms.[7] Stenoses are considered the most important cause of reconstruction failure.[11,14,16] In a recent randomized study intensive postoperative surveillance followed by correction of stenoses before occlusion has been shown to improve bypass patency.[19] It is generally agreed that isolated stenoses of greater than 50% diameter reduction and stenoses causing significant reduction of ankle/brachial index are associated with a high risk of bypass thrombosis and should be corrected.[11,19-21] It is important to assess whether a hemodynamic deterioration is caused by a stenosis or a distal fistula *and* a stenosis in combination. This distinction obviously determines the approach for intervention and most likely also the prognosis.

Because of its noninvasive nature ultrasound duplex scanning has become the preferred modality for postoperative surveillance of vein bypasses. Stenoses are detected by localized changes in the flow pattern, and arteriovenous fistulas are easily identified as patent side branches on the color Doppler image.[22] At present no ideal modality for quantification of fistulas is available. The fistula flow has been estimated by subtracting ultrasonically derived distal bypass flow from proximal bypass flow.[4] In small-caliber crural bypasses the value of this method is questionable.[23] Determination of proximal graft volume flow during distal obstruction gives a semiquantification of the flow capacity of the fistulas but not the actual fistula flow in the unobstructed graft.[6] Alternatively the degree of arteriovenous shunting can be assessed by means of radiolabeled albumin microspheres.[7] Because this method is invasive and associated with radiation, it has never gained widespread acceptance.

Several noninvasive methods are used for quantification of vein bypass stenoses. An interval reduction of ankle/brachial index exceeding 0.20 is used to separate trivial lesions from hemodynamically significant lesions in bypasses without fistulas.[24] According to our results, however, ankle/brachial index measurements could lead to an overestimation of the significance of stenoses in bypasses with distal fistulas. Consequently, subcritical stenoses may be misclassified as critical.

Low graft PSV has been claimed to identify failing grafts,[25] but PSV will be raised in the event of fistulas being present downstream of the measuring site, and the significance of stenoses may thus be underestimated. An end-diastolic velocity in a stenosis of more than 20 cm/sec discriminates between moderate ($\leq$70%) and severe (>70%) isolated stenoses,[26] but EDV is evidently increased in the presence of distal fistulas. The close correlation between pressure and Doppler waveform parameters found in this study suggests that Doppler spectra obtained distally in the bypass provide information only about the hemodynamic state of the limb but unfortunately not about the cause of a hemodynamic deterioration. A localized increase in PSV in the stenosis relative to PSV in a proximal vessel segment that has not undergone stenosis (PSV-ratio) is unaffected by the flow rate.[27]

Therefore determination of PSV-ratio may be assumed to be the best noninvasive method for quantification of stenoses occurring in combination with arteriovenous fistulas. A future expansion of this study could be simultaneous ultrasound velocity recordings before and during stenosis to estimate PSV-ratio.

Conclusion. The impact of bypass stenosis appears to be significantly affected by the presence of distal arteriovenous fistula that enhance the transstenostic pressure gradient and may lead to ischemia. In the evaluation of bypass stenoses it is imperative to disclose the presence of fistulas and if present, assess their contribution to peripheral hemodynamic impairment.

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